

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-20 (Cancelled)

21. (Previously presented): The method of claim 43 wherein the first and second cancer-specific nucleic acids are the same.

22. (Previously presented): The method of claim 43 wherein the first and second cancer-specific nucleic acids are different.

23. (Cancelled)

24. (Previously presented): The method of any one of claims 54-56 wherein the RNA comprises mRNA.

25. (Previously presented): The method of claim 24 wherein the mRNA is not expressed in the non-cancer cell.

26. (Previously presented): The method of claim 25 wherein the mRNA comprises all or a portion of a transcript of a gene selected from the group consisting of a CEA gene, a CK20 gene, a MUC1 gene, a tyrosinase gene and a MAGE3 gene.

27. (Previously presented): The method of any one of claims 54-56 wherein the DNA that is detected comprises genomic DNA selected from the group consisting of genomic DNA comprising a genomic mutation, genomic DNA comprising a gene that has undergone amplification, genomic DNA comprising a gene that has undergone loss of

heterozygosity, genomic DNA comprising a translocated gene and genomic DNA comprising a gene polymorphism.

28. (Previously presented): The method of any one of claims 54-56 wherein at least one nucleic acid that is detected comprises DNA, said DNA comprising genomic DNA selected from the group consisting of (i) the second cancer-specific nucleic acid and (ii) a cancer-associated nucleic acid that is present in at least one cancer cell in the second fraction.

29. (Previously presented): The method of any one of claims 54-56 wherein the DNA is genomic DNA that comprises all or a portion of an oncogene.

30. (Previously presented): The method of any one of claims 54-56 wherein the DNA is genomic DNA that comprises all or a portion of a tumor suppressor gene.

31. (Previously presented): The method of claim 27 wherein the genomic DNA comprises all or a portion of a gene selected from the group consisting of a p53 gene, an erb-B2 gene, a c-myc gene, a K-ras gene, an RB gene, an APC gene and a DCC gene.

32. (Previously presented): The method of any one of claims 41-43 wherein at least one nucleic acid selected from the group consisting of a (i) first cancer-associated nucleic acid and (ii) a second cancer-associated nucleic acid comprises a coding portion of a gene selected from the group consisting of a tissue-specific gene, a metastasis-associated gene, a steroid hormone receptor gene, a drug resistance gene, an immunomodulation gene, a cell proliferation gene and an apoptosis gene, or a complementary nucleic acid thereto.

33. (Previously presented): The method of claim 32 wherein the metastasis-associated gene encodes a gene product selected from the group consisting of an angiogenesis factor, a motility factor, a growth factor, a matrix degradation factor and an adhesion factor.

34. (Previously presented): The method of claim 33 wherein the matrix degradation factor is selected from the group consisting of a proteinase and a proteinase inhibitor.

35. (Previously presented): The method of claim 33 wherein the adhesion factor is an adherin.

36. (Previously presented): The method of claim 24 wherein the mRNA encodes a gene product selected from the group consisting of bFGF, bFGF-R, VEGF, VEGF-R1, VEGF-R2, MMP2 and TIMP3.

37. (Previously presented): The method of any one of claims 41-43 wherein the cancer cell is removed from the body fluid by a method selected from the group consisting of microfiltration, density gradient centrifugation and antigen-specific immunoadsorption.

38. (Previously presented): A method for identifying an anticancer therapy, comprising:

(a) detecting, before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell,

(i) in a plurality of cells obtained from a body fluid of the subject, an absence or presence of at least one nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid, said plurality of cells comprising at least one cancer cell and at least one non-cancer cell;

(ii) in at least one cancer cell removed from said plurality of cells, the absence or presence of at least one nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid; and

(iii) in at least one non-cancer cell from the subject, the absence or presence of said nucleic acids from step (i) and step (ii),

wherein said first and second cancer-specific nucleic acids are different,
and wherein said first and second cancer-associated nucleic acids are different; and

(b) determining, after administering the candidate anticancer therapy, a decreased presence of said nucleic acids in said cancer cell relative to the presence or absence of said nucleic acids in said non-cancer cell, and therefrom identifying an anticancer therapy.

39. (Previously presented): A method for identifying an anticancer agent, comprising:

(a) detecting in at least one cell, before and after contacting a candidate anticancer agent with a plurality of cells known to include or suspected of including a disseminated cancer cell or a micrometastasized cancer cell,

(i) an absence or presence of at least one nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid, and

(ii) in at least one cancer cell removed from said plurality of cells, the absence or presence of at least one nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid, and

(iii) in at least one non-cancer cell from said plurality of cells, the absence or presence of said nucleic acids from step (i) and step (ii),

wherein said first and second cancer-specific nucleic acids are different, and wherein said first and second cancer-associated nucleic acids are different; and

(b) determining, after contacting the candidate anticancer therapy with the cells, a decreased presence of any one or more of said nucleic acids in said cancer cell relative to the presence or absence of said nucleic acids in the non-cancer cell, and therefrom identifying an anticancer agent.

40. (Cancelled)

41. (Currently Amended): A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

~~(a) dividing-detecting in a plurality of cells into at least a first fraction and a second fraction obtained~~, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the first fraction has not been subjected to a method for isolating cancer cells from non-cancer cells, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

~~(b) detecting in the first fraction an absence or presence of at least one first nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid, wherein the body fluid has not been subjected to a method for isolating cancer cells from non-cancer cells, and wherein the first cancer-associated nucleic acid is not expressed in the non-cancer cells;~~

~~(b) isolating from the body fluid at least one cancer cell according to a method for removing cancer cells from non-cancer cells;~~

~~(c) detecting, in the second fraction, in at least one cancer cell removed from the body fluid, an absence or presence of at least one second nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid;~~
and

~~(d) detecting in at least one non-cancer cell from the subject body fluid an absence or presence of the at least one second nucleic acid that is detected in step (c),~~

wherein said first and second cancer-specific nucleic acids are different, wherein said first and second cancer-associated nucleic acids are different, wherein the presence of said first nucleic acid in the ~~first fraction~~ plurality of cells and an increased or decreased presence of the second nucleic acid in ~~said second fraction~~ the cancer cell relative to the presence or absence of said second nucleic acid in the non-cancer cell from the ~~subject body fluid~~ indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

42. (Currently Amended): A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) ~~dividing~~ detecting in a plurality of cells obtained into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, an absence or presence of at least one first cancer-specific nucleic acid, and wherein the first fraction ~~body fluid~~ has not been subjected to a method for isolating cancer cells from non-cancer cells, ~~and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;~~

(b) isolating from the body fluid at least one cancer cell according to a method for removing cancer cells from non-cancer cells;

(c) detecting in the second fraction at least one cancer cell removed from the body fluid an absence or presence of at least one second cancer-specific nucleic acid; and

(d) detecting in at least one non-cancer cell from the subject body fluid an absence or presence of the second cancer-specific nucleic acid that is detected in step (c),

wherein said first and second cancer-specific nucleic acids are different, wherein the presence of said first cancer-specific nucleic acid in ~~said first fraction~~ the plurality of cells and an increased or decreased presence of said second cancer-specific nucleic acid in ~~said second fraction~~ the cancer cell relative to the presence or absence of said second cancer-specific nucleic acid in a non-cancer cell from the ~~subject body fluid~~ indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

43. (Currently Amended): A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) ~~dividing~~ detecting in a plurality of cells obtained into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for

having a disseminated cancer cell or a micrometastasized cancer cell, an absence or presence of at least one first cancer-specific nucleic acid, ~~and wherein the first fraction~~ body fluid has not been subjected to a method for isolating cancer cells from non-cancer cells, ~~and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;~~

~~(b) detecting in the first fraction an absence or presence of at least one first cancer-specific nucleic acid;~~

(b) isolating from the body fluid at least one cancer cell according to a method for removing cancer cells from non-cancer cells;

~~(c) detecting in the second fraction~~ at least one cancer cell removed from the body fluid an absence or presence of at least one second cancer-specific nucleic acid;

(d) detecting an absence or presence of at least one cancer-associated nucleic acid in at least one sample selected from the group consisting of (i) the first fraction plurality of cells and (ii) ~~the second fraction~~ at least one cancer cell removed from the body fluid; and

(e) detecting in at least one non-cancer cell from the subject an absence or presence of said second cancer-specific nucleic acid detected in step (c) and said cancer-associated nucleic acid detected in step (d),

wherein the presence of said first cancer-specific nucleic acid and of said cancer-associated nucleic acid in ~~said first fraction~~ the plurality of cells and an increased or decreased presence of said second cancer-specific nucleic acid and of said cancer-associated nucleic acid in ~~said second fraction~~ the cancer cell relative to the presence or absence of said second cancer-specific nucleic acid and of said cancer-associated nucleic acid in a non-cancer cell from the ~~subject body fluid~~ indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

44. (Previously presented): The method of any one of claims 41-43 wherein a nucleic acid selected from the group consisting of (i) a first cancer-specific nucleic acid and (ii) a first cancer-associated nucleic acid comprises an organotypical gene, and wherein the presence of at least one of said first nucleic acids comprising an organotypical gene indicates the type of malignant disease from which the cancer cell is derived.

45. (Previously presented): The method of claim 41 wherein a nucleic acid selected from the group consisting of (i) a first cancer-associated nucleic acid and (ii) a second cancer-associated nucleic acid, said nucleic acid comprising a metastasis-associated gene, and wherein the presence of said first cancer-associated nucleic acid comprising the metastasis-associated gene indicates an increased risk that a disseminated cancer cell has the ability to metastasize, and wherein an increased or decreased presence of said second cancer-associated nucleic acid comprising the metastasis-associated gene in said cancer cell relative to the presence or absence of said second cancer-associated nucleic acid comprising the metastasis-associated gene in a non-cancer cell from the subject indicates an increased risk that a disseminated cancer cell has the ability to metastasize.

46. (Previously presented): The method of either claim 45 or claim 60 wherein the metastasis-associated gene encodes a gene product selected from the group consisting of an angiogenesis factor, a motility factor, a growth factor, a matrix degradation factor and an adhesion factor.

47. (Previously presented): The method of claim 46 wherein the matrix degradation factor is selected from the group consisting of a proteinase and a proteinase inhibitor.

48. (Previously presented): The method of claim 46 wherein the adhesion factor is an adherin.

49. (Previously presented): The method of either claim 45 or claim 60 wherein the nucleic acid is selected from the group consisting of DNA and RNA.

50. (Previously presented): The method of claim 49 wherein the RNA comprises mRNA.

51. (Previously presented): The method of claim 50 wherein the mRNA encodes a gene product selected from the group consisting of bFGF, bFGF-R, VEGF, VEGF-R1, VEGF-R2, MMP2 and TIMP3.

52. (Previously presented): The method according to any one of claims 41-42 wherein steps (a) - (d) are performed before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell.

53. (Previously presented): The method according to claim 43 wherein steps (a) - (e) are performed before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell.

54. (Previously presented): The method of claim 41 wherein the first nucleic acid is RNA and wherein the second nucleic acid is selected from the group consisting of DNA and RNA.

55. (Previously presented): The method of claim 42 wherein the first cancer-specific nucleic acid is RNA and wherein the second cancer-specific nucleic acid is selected from the group consisting of DNA and RNA.

56. (Previously presented): The method of claim 43 wherein the first cancer-specific nucleic acid is selected from the group consisting of DNA and RNA, wherein the second cancer-specific nucleic acid is selected from the group consisting of DNA and RNA, and wherein the cancer-associated nucleic acid is selected from the group consisting of DNA and RNA.

57. (Previously presented): The method of claim 44 wherein the organotypical gene encodes an organotypical marker.

58. (Previously presented): The method of claim 44 wherein the first nucleic acid is RNA.

59. (Previously presented): The method of claim 58 wherein the RNA comprises mRNA.

60. (Previously presented): The method of claim 43 wherein the cancer-associated nucleic acid comprises a metastasis-associated gene, and wherein the presence of the cancer-associated nucleic acid comprising the metastasis-associated gene indicates an increased risk that a disseminated cancer cell has the ability to metastasize, and wherein an increased or decreased presence of the cancer-associated nucleic acid comprising the metastasis-associated gene in said cancer cell relative to the presence or absence of the cancer-associated nucleic acid comprising the metastasis-associated gene in a non-cancer cell from the subject indicates an increased risk that a disseminated cancer cell has the ability to metastasize.

61.-68. (Not entered)